Application No.: 09/942,458

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

In the claims

Claim 1 (currently amended): An echinocandin/carbohydrate complex comprising a carbohydrate complexed with an echinocandin compound represented by the following structure:

wherein:

R is an alkyl group, an alkenyl group, an alkynyl group, an aryl group, heteroaryl group, or combinations thereof;

 R_1 , R_2 , R_3 , R_6 , R_7 , and R_{10} are independently hydroxy or hydrogen;

R₄ is hydrogen, methyl or -CH₂C(O)NH₂;

R₅ and R₁₁ are independently methyl or hydrogen;

 R_8 is -OH, -OSO₃H, -OPO₃H₂, -OPO₃HR^a, or -OPO₂HR^a, where R^a is hydroxy, C₁-C₆ alkyl, C₁-C₆ alkoxy, phenyl, phenoxy, p-halophenyl, p-halophenoxy, p-nitrophenyl, p-nitrophenoxy, benzyl, benzyloxy, p-halobenzyl, p-halobenzyloxy, p-nitrobenzyl, or p-nitrobenzyloxy;

R₉ is -H, -OH, or -OSO₃H; and pharmaceutically acceptable salts or hydrates thereof;

wherein the carbohydrate is released upon dispersion of the of the echinocandin/carbohydrate complex in water.

Claim 2 (original): The complex of Claim 1 wherein

 R_4 , R_5 and R_{11} are each methyl;

R₂ and R₇ are independently hydrogen or hydroxy; R₁, R₃, R₆ and R₁₀ are each hydroxy;

R₈ is -OH, -OPO₃HR^a, or -OPO₂HR^a, where R^a is methyl;

R is linoleoyl, palmitoyl, stearoyl, myristoyl, 12-methylmyristoyl, 10,12-dimethylmyristoyl, or a group having the general structure:

$$A$$
,
 A ,
 B ,
 C , or
 C

where A, B, C and D are independently hydrogen, C_1 - C_{12} alkyl, C_2 - C_{12} alkynyl, C_1 - C_{12} alkoxy, C_1 - C_{12} alkylthio, halo, or -O-(CH₂)_m-[O-(CH₂)_n]_p-O-(C₁-C₁₂ alkyl) or -O-(CH₂)_q-X-E; m is 2, 3 or 4;

n is 2, 3 or 4; p is 0 or 1; q is 2, 3 or 4;

X is pyrrolidino, piperidino or piperazino;

E is hydrogen, C_1 - C_{12} alkyl, C_3 - C_{12} cycloalkyl, benzyl or C_3 - C_{12} cycloalkylmethyl.

Claim 3 (original): The complex of claim 2 wherein

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 R_2 and R_7 are each hydroxy; R_8 is hydroxy; and

Claim 4 (original): The complex of Claim 1 wherein said carbohydrate is selected from the group consisting of adonitol, arabinose, arabitol, ascorbic acid, chitin, D-cellubiose, 2-deoxy-D-ribose, dulcitol, (S)-(+)-erythrulose, fructose, fucose, galactose, glucose, inositol, lactose, lactulose, lyxose, maltitol, maltose, maltotriose, mannitol, mannose, melezitose, melibiose, microcrystalline cellulose, palatinose, pentaerythritol, raffinose, rhamnose, ribose, sorbitol, sorbose, starch, sucrose, trehalose, xylitol, xylose and hydrates thereof.

Claim 5 (original): The complex of Claim 3 wherein said carbohydrate is selected from the group consisting of L-arabinose, D-arabitol, L-arabitol, 2-deoxy-D-ribose, (S)-(+)-erythrulose, D-fructose, D-(+)-fucose, L-fucose, D-galactose, α-D-glucose, β-D-glucose, L-glucose, D-lyxose, L-lyxose, maltitol, D-maltose, maltotriose, D-mannose, melezitose, palatinose, D-raffinose, L-rhamnose, D-ribose, D-sorbitol, D-trehalose, xylitol, L-xylose and hydrates thereof.

Claim 6 (original): The complex of Claim 5 wherein said carbohydrate is selected from the group consisting of L-arabinose, D-arabitol, L-arabitol, 2-deoxy-D-ribose, (S)-(+)-erythrulose, D-fructose, D-(+)-fucose, L-fucose, D-galactose, β -D-glucose, D-lyxose, L-lyxose, D-maltose, maltotriose, melezitose, palatinose, D-raffinose, D-sorbitol, D-trehalose, xylitol, L-xylose and hydrates thereof.

Claim 7 (withdrawn – currently amended): A Echinocandin/carbohydrate crystalline complex prepared by the steps of:

(a) providing an echinocandin compound represented by the following structure

 R_2 and R_7 are each hydroxy;

R₈ is hydroxy; and

$$R = O(CH_2)_4 CH_3$$

Claim 4 (original): The complex of Claim 1 wherein said carbohydrate is selected from the group consisting of adonitol, arabinose, arabitol, ascorbic acid, chitin, D-cellubiose, 2-deoxy-D-ribose, dulcitol, (S)-(+)-erythrulose, fructose, fucose, galactose, glucose, inositol, lactose, lactulose, lyxose, maltitol, maltose, maltotriose, mannitol, mannose, melezitose, melibiose, microcrystalline cellulose, palatinose, pentaerythritol, raffinose, rhamnose, ribose, sorbitol, sorbose, starch, sucrose, trehalose, xylitol, xylose and hydrates thereof.

Claim 5 (original): The complex of Claim 3 wherein said carbohydrate is selected from the group consisting of L-arabinose, D-arabitol, L-arabitol, 2-deoxy-D-ribose, (S)-(+)-erythrulose, D-fructose, D-(+)-fucose, L-fucose, D-galactose, α-D-glucose, β-D-glucose, L-glucose, D-lyxose, L-lyxose, maltitol, D-maltose, maltotriose, D-mannose, melezitose, palatinose, D-raffinose, L-rhamnose, D-ribose, D-sorbitol, D-trehalose, xylitol, L-xylose and hydrates thereof.

Claim 6 (original): The complex of Claim 5 wherein said carbohydrate is selected from the group consisting of L-arabinose, D-arabitol, L-arabitol, 2-deoxy-D-ribose, (S)-(+)-erythrulose, D-fructose, D-(+)-fucose, L-fucose, D-galactose, β-D-glucose, D-lyxose, L-lyxose, D-maltose, maltotriose, melezitose, palatinose, D-raffinose, D-sorbitol, D-trehalose, xylitol, L-xylose and hydrates thereof.

Claim 7 (withdrawn): A Echinocandin/carbohydrate crystalline complex prepared by the steps of:

(a) providing an echinocandin compound represented by the following structure

wherein

R is an alkyl group, an alkenyl group, an alkynyl group, an aryl group, heteroaryl group, or combinations thereof,

R₁, R₂, R₃, R₆, R₇, and R₁₀ are independently hydroxy or hydrogen,

R₄ is hydrogen, methyl or -CH₂C(O)NH₂,

R₅ and R₁₁ are independently methyl or hydrogen,

 R_8 is -OH, -OSO₃H, -OPO₃H₂, -OPO₃HR^a, or -OPO₂HR^a, where R^a is hydroxy, C₁-C₆ alkyl, C₁-C₆ alkoxy, phenyl, phenoxy, *p*-halophenyl, *p*-halophenoxy, *p*-nitrophenyl, *p*-nitrophenoxy, benzyl, benzyloxy, *p*-halobenzyloxy, *p*-nitrobenzyl, or *p*-nitrobenzyloxy;

R₉ is -H, -OH, or -OSO₃H, and

pharmaceutically acceptable salts or hydrates thereof;

(b) mixing together said echinocandin compound of step (a) to a carbohydrate in a solvent to form a mixture;

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(c) heating said mixture to solubilize said echinocandin compound and to solubilize or disperse said carbohydrate;

- (d) allowing said mixture to cool to produce said echinocandin/carbohydrate complex; and
 - (e) isolating said echinocandin/carbohydrate complex;

wherein said echinocandin/carbohydrate complex is characterized by the carbohydrate being released upon dispersion of the of the echinocandin/carbohydrate complex in water.

Claim 8 (withdrawn): The complex of Claim 7 wherein

 R_4 , R_5 and R_{11} are each methyl;

R₂ and R₇ are independently hydrogen or hydroxyl; R₁, R₃, R₆ and R₁₀ are each hydroxy;

 R_8 is -OH, -OPO₃HR^a, or -OPO₂HR^a, where R^a is methyl;

R is linoleoyl, palmitoyl, stearoyl, myristoyl, 12-methylmyristoyl, 10, 12-dimethylmyristoyl, or a group having the general structure:

where A, B, C, and D are independently hydrogen, C_1 - C_{12} alkyl, C_2 - C_{12} alkynyl, C_1 - C_{12} alkoxy, C_1 - C_{12} alkylthio, halo, or -O-(CH₂)_m-[O-(CH₂)_n]_p-O-(C₁-C₁₂ alkyl) or -O-(CH₂)_q-X-E;

m is 2, 3 or 4;

n is 2, 3, or 4; p is 0 or 1; q is 2, 3 or 4;

X is pyrrolidino, piperidino or piperazino;

E is hydrogen, C₁-C₁₂ alkyl, C₃-C₁₂ cycloalkyl, benzyl or C₃-C₁₂ cycloalkylmethyl.

Claim 9 (withdrawn): The complex of claim 8 wherein

R₂ and R₇ are each hydroxyl;

R₈ is hydroxyl; and

$$R = O(CH_2)_4 CH_3$$

Claim 10 (withdrawn): The complex of Claim 7 wherein said carbohydrate is selected from the group consisting of adonitol, arabinose, arabitol, ascorbic acid, chitin, D-cellubiose, 2-deoxy-D-ribose, dulcitol, (S)-(+)-erythrulose, fructose, fucose, galactose, glucose, inositol, lactose, lactulose, lyxose, maltitol, maltose, maltotriose, mannitol, mannose, melezitose, melibiose, microcrystalline cellulose, palatinose, pentaerythritol, raffinose, rhamnose, ribose, sorbitol, sorbose, starch, sucrose, trehalose, xylitol and hydrates thereof.

Claim 11 (withdrawn): The complex of Claim 9 wherein said carbohydrate is selected from the group consisting of L-arabinose, D-arabitol, L-arabitol, 2-deoxy-D-ribose, (S)-(+)-erythrulose, D-fructose, D-(+)-fucose, L-fucose, D-galactose, α-D-glucose, β-D-glucose, L-glucose, D-lyxose, L-lyxose, maltitol, D-maltose, maltotriose, D-mannose, melezitose, palatinose, D-raffinose, L-rhamnose, D-ribose, D-sorbitol, D-trehalose, xylitol, L-xylose and hydrates thereof.

Claim 12 (withdrawn): The complex of Claim 9 wherein said carbohydrate is selected from the group consisting of L-arabinose, D-arabitol, L-arabitol, 2-deoxy-D-ribose, (S)-(+)-erythrulose, D-fructose, D-(+)-fucose, L-fucose, D-galactose, β-D-glucose, D-lyxose, L-lyxose, D-maltose,

maltotriose, melezitose, palatinose, D-raffinose, D-sorbitol, D-trehalose, xylitol, L-xylose and hydrates thereof.

Claim 13 (withdrawn): The complex of Claim 7 wherein said solvent is selected from the group consisting of methanol, ethanol, benzyl alcohol, mixtures of benzyl alcohol with methanol, ethanol, n-propanol, isopropanol, n-butanol, 2-butanol, 2-pentanol, 2-methyl-1-propanol, MEK, acetone, ethyl acetate, toluene, acetonitrile, fluorobenzene, methylene chloride, nitromethane, cyclopentanone and cyclohexanone.

Claim 14 (withdrawn): The complex of Claim 13 wherein said solvent is selected from the group consisting of methanol, ethanol, benzyl alcohol, and mixtures of benzyl alcohol with methyl ethyl ketone, ethyl acetate, and acetonitrile.

Claim 15 (withdrawn): The complex of Claim 14 wherein said solvent is methanol.

Claim 16 (withdrawn): The complex of Claim 15 wherein said carbohydrate is soluble in said methanol when heated to about 40° to 60°C.

Claim 17 (withdrawn): The complex of Claim 15 wherein said carbohydrate is highly soluble in said methanol when heated to about 40° to 60°C.

Claim 18 (withdrawn): The complex of Claim 15 wherein said carbohydrate is insoluble in said methanol when heated to about 40° to 60°C.

Claim 19 (withdrawn): The complex of Claim 7 wherein said carbohydrate co-crystallizes with said echinocandin compound.

Claim 20 (original): A process for preparing a parenteral formulation comprising the step of (i) mixing the echinocandin/carbohydrate complex of Claim 1 in an aqueous solvent.

Claim 21 (original): The process of Claim 20 further comprising the steps of (ii) sterile filtering and (iii) freeze-drying.

Claim 22 (original): A pharmaceutical formulation comprising the echinocandin/carbohydrate complex of Claim 1 and a pharmaceutically acceptable excipient.

Claim 23 (original): The pharmaceutical formulation of Claim 22 wherein said excipient is selected from the group consisting of tonicity agents, stabilizing agents, buffers, bulking agents surfactants, and combinations thereof.

Claim 24 (withdrawn): A method for treating a fungal infection in a mammal in need thereof, which comprises administering to said mammal the echinocandin/carbohydrate complex of Claim 1.

Claim 25 (withdrawn): The method of Claim 24 wherein said fungal infection arises from *Candida* albicans or *Aspergillus fumigatis* activity.

Claim 26 (withdrawn – currently amended): A method for treating an antifungal a fungal infection in a mammal in need thereof, which comprises contacting a the echinocandin/carbohydrate complex of Claim 1 with bodily fluids of said mammal, wherein said complex collapses to an amorphous form when contacted with said bodily fluids.

Claim 27 (withdrawn): The method of Claim 26 wherein said fungal infection arises from *Candida* albicans or *Aspergillus fumigatis* activity.

Claim 28 (new): The complex of Claim 1 wherein the complex is crystalline.

Claim 29 (new): The complex of Claim 1 wherein the carbohydrate is fructose.

Claim 30 (new): The complex of Claim 3 wherein the carbohydrate is fructose.

Claim 31 (new): The complex of Claim 28 wherein the carbohydrate is fructose.

Claim 32 (new): The complex of Claim 30 wherein the complex is crystalline.

Claim 33 (new): A pharmaceutical formulation comprising the echinocandin/carbohydrate complex of Claim 28 and a pharmaceutically acceptable excipient.

Claim 34 (new): A pharmaceutical formulation comprising the echinocandin/carbohydrate complex of Claim 30 and a pharmaceutically acceptable excipient.

Claim 35 (new): A method for treating a fungal infection in a mammal in need thereof, which comprises administering to said mammal the echinocandin/carbohydrate complex of Claim 28.

Claim 36 (new): A method for treating a fungal infection in a mammal in need thereof, which comprises administering to said mammal the echinocandin/carbohydrate complex of Claim 30.

Claim 37 (new): A method for treating a fungal infection in a mammal in need thereof, which comprises administering to said mammal the echinocandin/carbohydrate complex of Claim 32.

Claim 38 (new): A method for treating a fungal infection in a mammal in need thereof, which comprises contacting the echinocandin/carbohydrate complex of Claim 28 with bodily fluids of said mammal, wherein said complex collapses to an amorphous form when contacted with said bodily fluids.

Claim 39 (new): A method for treating a fungal infection in a mammal in need thereof, which comprises contacting the echinocandin/carbohydrate complex of Claim 30 with bodily fluids of said mammal, wherein said complex collapses to an amorphous form when contacted with said bodily fluids.

Claim 40 (new): A method for treating a fungal infection in a mammal in need thereof, which comprises contacting the echinocandin/carbohydrate complex of Claim 32 with bodily fluids of said mammal, wherein said complex collapses to an amorphous form when contacted with said bodily fluids.